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Sleep disorders in children with cerebral palsy: neurodevelopmental and behavioral correlates

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ABSTRACT

Objectives: We aimed to estimate the frequency of sleep disorders in children with cerebral palsy (CP) using the Sleep Disturbance Scale for Children (SDSC) and to evaluate the relations between sleep disorders and motor, cognitive, and behavioral problems.
Methods: One hundred and sixty-five children with CP ages 6–16 years (mean age, 11 years) were assessed using the SDSC, the Gross Motor Function Classification System (GMFCS), the Wechsler Intelligence Scale for Children and the Child Behavior Check List (CBCL) to assess sleep, motor, cognitive, and behavioral problems, respectively.
Results: An abnormal total sleep score was found in 19% of children with CP; more than 40% of children had an abnormal score on at least one SDSC factor. The SDSC total score was significantly associated ($P < .01$) with mental retardation, epilepsy, CBCL scores, and level 5 on the GMFCS.
Conclusions: Our results confirm that sleep disorders are common in children with cerebral palsy. The relationship between motor and cognitive behavior and epilepsy should be further explored to better understand how these factors influence one another to identify effective treatments and to improve the well-being of the child.

1. Introduction

Sleep disorders represent a common problem in infancy and childhood [1–5]. In healthy children, the prevalence of sleep disorders can vary from 5% to 40% [3–5]. This wide range of prevalence is most likely due to the absence of a consensus on what threshold constitutes clinical sleep pathology, the different sample characteristics, the various instruments used to assess sleep, and the duration criteria for defining a sleep problem [6].

Although there are several studies assessing sleep in children with developmental disabilities [6–13], there are only a few in children with cerebral palsy (CP) [6,11–13]; these few studies have reported that sleep disorders are more frequent in CP than in typically developing children. The increased prevalence was related to muscle spasms, musculoskeletal pain, and epilepsy. Newman et al. [6] reported data on 173 children with different types of CP, with 44% of the children presenting with at least one clinically significant sleep disorder. However, the authors did not consider the presence of mental retardation and behavioral problems, which are known to have a strong influence on sleep [1–9,11,12]. The relationship between sleep and behavior in CP has never been systematically addressed. This issue is particularly relevant, as there is increasing evidence of the high prevalence of behavior problems in children with CP ranging from 26% to 80% [14,15]. Because it is known that sleep disturbances can greatly affect daytime behavior in children leading to neurobehavioral disturbances (e.g., inattention, hyperactivity, learning problems) [1–3,10], we hypothesized that sleep disturbances may be related to daytime behavior in children with CP.

The aims of our study were to estimate the frequency of sleep disorders in children with CP after the age of 6 years and to evaluate the relationship between sleep disorders and motor, cognitive, and behavioral problems.

2. Methods

The children included in our study were part of a collaborative prospective project on families of children with CP regularly

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followed at the Child Neurology Unit of the Catholic University of Rome and the Neurological Institute Besta in Milan, Italy, between January 2010 and December 2012. To have a homogeneous cohort, we only included children with no parental history of a severe or chronic medical condition (e.g., stroke, diabetes mellitus) or a psychologic disorder. The inclusion criteria were children with a diagnosis of CP between the ages of 6 and 16 years with a detailed cognitive and motor assessment. The age range was based on the choice of some assessments performed in the study, for which validation studies and normative data are available from the age of 6 years.

CP was defined as a group of disorders in the development of movement and posture, causing activity limitation attributed to nonprogressive disturbances occurring in the developing fetal or infant brain [16]. Clinical diagnosis was based on the predominant type of motor impairment and was classified according to the criteria proposed by Himmelmann et al. [17]. The children were divided into four groups according to the type of CP: diplegia, hemiplegia, quadriplegia and dyskinesia. All children with CP underwent a comprehensive assessment of motor, cognitive, and behavioral abilities and sleep disturbances. Motor function was evaluated using the Gross Motor Function Classification System (GMFCS) [18] to classify each child's level of gross motor function, with skill levels from 1 to 2 assessing the children's gross motor function by observation.

Cognitive function was measured by using the Wechsler Intelligence Scale for Children III-Revised [19] for children between the ages of 6 and 16 years. The test was performed by a trained psychologist for all the children. Child behavior was assessed using the Child Behavior Check List (CBCL) [20,21]. In this test behavior problems are reported by the child's primary caregiver, the individual who is most responsible for the day-to-day decision making and care of the child. The CBCL consists of 118 items on which parents rate their child's behavior by using 3-point scales: 0 (not true), 1 (somewhat or sometimes true), and 2 (very true or often true). The CBCL provides a total behavior problems score, 2 second-order factor scores (internalizing problems, externalizing problems), and 8 syndrome scores (aggressive behavior, anxious/depressed, attention problems, delinquent behavior, social problems, thought problems, withdrawn, somatic complaints). Raw scores on each clinical factor were transformed to T scores based on published norms. Scores higher than 63 were considered abnormal, scores between 60 and 63 were considered borderline, and scores of less than 60 were considered normal.

Sleep disturbances were assessed using the Sleep Disturbance Scale for Children (SDSC), which showed thorough validation, an adequate level of internal consistency, test–retest reliability, and availability of normative data [3,10]. This scale was originally validated on a sample of 1157 healthy children from the general population aged 6–16 years. It investigates the occurrence of sleep disorders during the previous 6 months and contains 26 items in a Likert-type scale with values from 1 to 5; higher numerical values reflect a higher clinical severity of symptoms. The sum of scores provided a total sleep score with a possible range from 26 to 130. A T score of more than 70 (>95th centile) was regarded as abnormal, and a score of 70 or less was considered to be normal.

The original factor analysis yielded six sleep disturbance factors representing the most common areas of sleep disorders in childhood and adolescence: (1) disorders of initiating and maintaining sleep; (2) sleep-breathing disorders; (3) disorders of arousal, including sleepwalking, sleep terrors, and nightmares; (4) sleep–wake transition disorders (SWTD), including hypnic jerks, rhythmic movement disorders, hypnagogic hallucinations, nocturnal hyperkinesias, and bruxism; (5) disorders of excessive somnolence; and (6) sleep hyperhidrosis (SHY).

This questionnaire was distributed to the primary caregiver of children during the routine neurologic assessment in our units. This questionnaire was completed together with information on the parents' marital status and current parental employment. These demographic data were only used to assess statistical differences between the four CP groups on the requested information. The children also were screened for the presence of epilepsy, which was further categorized into controlled or intractable/active when the seizures were not controlled with treatment, and antiepileptic therapy.

The study protocol was approved by the ethics committee of the institutions and informed consent was obtained from parents.

2.1. Statistical analysis

The children were divided into four groups according to the type of CP. Data were presented as mean values (standard deviations [SDs]) for continuous normally distributed variables, median (interquartile range) for normal continuous variables, and numbers and percentages for categorical variables. The comparisons of the continuous variables, including children's ages, cognitive assessments, scores on SDSC total, and six factors on CBCL scales, were performed using the Kruskal–Wallis equality of populations rank test; the comparisons of the categorical variables (gender, demographic factors, controlled or active epilepsy) and GMFCS scores were performed with the Fisher exact test.

The correlation between SDSC total score and CBCL total scores was explored with Spearman rank order correlation test. Dummy variables for abnormal scores and CBCL scores were created and the association between an abnormal total SDSC score and the physical parameters (i.e., sex, age, CP type, developmental delay, GMFCS level, epilepsy, abnormal CBCL scores) were performed and reported as crude odds ratios (OR) with 95% confidence intervals (CI) and OR adjusted for type of cerebral palsy.

Multivariate analysis was conducted using logistic regression analyses to define the role of specific factors which may affect an abnormal total SDSC score. All of the variables were entered into the initial model. Backward stepwise selection was used to select the variables to enter in the final model with a significance level for the removal and the addition of .3 and .2, respectively. Results of the logistic regression analyses are expressed as OR with 95% CI. A two-tailed value of $P < .05$ was considered significant. Statistical analysis was performed using the Stata Statistical Software: Release 10 (StataCorp LP, College Station, TX).

3. Results

During the study period, 165 children with CP (99 boys; 66 girls) and the primary caregiver fulfilled the inclusion criteria. There were 38 children who presented diplegia (25 boys; 13 girls), 56 presented with hemiplegia (37 boys; 19 girls), 64 presented with quadriplegia (33 boys; 31 girls), and 7 presented with dyskinesia (4 boys; 3 girls). The mean age was 11 years (range, 6–16 years). Sixty-three children were affected by epilepsy (39 with quadriplegia, 17 with hemiplegia, 4 with diplegia, and 3 with dyskinesia) and were all receiving antiepileptic medication. Forty-one out of 63 children showed intractable/active epilepsy (33 quadriplegia, 5 hemiplegia, 2 dyskinesia, 1 diplegia). No statistical difference was found between the mean ages of children in the various forms of CP. No difference was identified in demographic factors or gender (Table 1).

3.1. Cognitive and motor function

Table 2 reports the distribution of motor and cognitive function in children with CP.

Table 1
Demographic factors.

	Diplegia (*n*)	Hemiplegia (*n*)	Quadriplegia (*n*)	Dyskinesia (*n*)	Total
Parents' marital status					
Single	4	7	8	1	20
Married/cohabiting	34	49	56	6	145
Parents' employment status					
Unemployed	3	5	5	0	13
Employed (both/single)	35	51	59	7	152

Table 2
Distribution of subjects based on motor and cognitive functioning.

	Diplegia (*n*)	Hemiplegia (*n*)	Quadriplegia (*n*)	Dyskinesia (*n*)	Total (*n*) (%)
GMFCS level					
1	15	52	1	0	68 (41)
2	12	4	2	2	20 (12)
3	11	0	8	0	19 (12)
4	0	0	15	2	17 (10)
5	0	0	38	3	41 (25)
IQ					
In reference range	19	33	2	0	54 (33)
Borderline	7	7	6	0	20 (12)
Mental retardation	12	16	56	7	91 (55)
Total (*N*) (%)	38 (23)	56 (34)	64 (39)	77 (4)	165 (100)

Abbreviations: GMFCS, Gross Motor Function Classification System; IQ, intelligence quotient.

Regarding motor functions, children with hemiplegia were mainly in level 1 on the GMFCS; children with diplegia were equally distributed in levels 1–3, whereas children with quadriplegia were in levels 4 and 5. Regarding cognitive functions, children with hemiplegia and diplegia reported a normal intelligence quotient (IQ) in approximately 50%, whereas children with quadriplegia exhibited a mental retardation in more than 85%. Children with quadriplegia showed a significantly lower IQ ($P < .001$) and a higher GMFCS level than children with diplegia or hemiplegia.

3.2. CBCL results

All the caregivers completed the questionnaire. Details of the scores of the CBCL reported by the primary caregiver (mother in all cases) are reported in Table 3. Almost all children with diplegia, hemiplegia, and quadriplegia had median total internalizing and externalizing scores within reference range; the whole group of children with CP showed pathologic scores in the 24%, 27%, and 9%, respectively, for total, internalizing, and externalizing scores. No significant difference was reported among the four groups ($P > .05$) for total CBCL scores. In internalizing domains, children with dyskinetic CP showed statistically significant higher scores ($P < .05$) than hemiplegia, quadriplegia, and diplegia, while children with hemiplegia and dyskinetic CP showed statistically significant higher scores than children with diplegia and quadriplegia in the externalizing domain ($P < .01$).

3.3. SDSC results

An abnormal total sleep score (>70) was found in 31 children with CP (19%). Approximately 42% had an abnormal score on at least one SDSC factor: disorders of initiating and maintaining sleep (22%), sleep-breathing disorders (14%), disorders of arousal (10%), SWTD (15%), disorders of excessive somnolence (13%), and SHY (7%). On intergroup comparison, dyskinetic CP children presented higher significant scores for SWTD ($P < .05$) and SHY ($P < .01$) than children with hemiplegia, quadriplegia, or diplegia.

On univariate analysis (crude OR and adjusted OR) an abnormal total sleep score (Table 4) was significantly associated with mental retardation, presence of epilepsy (controlled or active), CBCL scores (externalizing, internalizing, and total score), and level 5 on the GMFCS (only for crude OR) ($P < .01$). On multivariate analysis (Table 5), the final model selected the variables mental retardation, active epilepsy, abnormal internalizing and externalizing scores on the CBCL, and level 5 on the GMFCS. An abnormal total SDSC score was only significantly associated with the presence of abnormal CBCL scores, both internalizing and externalizing ($P < .01$).

Table 6 reported the incidence of abnormal SDSC scores related to the associated clinical factors (cognitive and motor function, behavior, and epilepsy). Of the 31 children with an abnormal SDSC total score, 14 presented active epilepsy, 4 controlled epilepsy, and 13 showed no signs of epilepsy. No specific relationship was observed between the type of antiepileptic agent and SDSC scores (Table 7). According to motor and cognitive function, 24 children showed mental retardation and 15 children showed a level 5 on GMFCS. On the CBCL, 11 children showed a score within the reference range and the other 20 showed an abnormal score.

3.4. SDSC and CBCL scores correlation

A moderate correlation was found between SDSC total score and CBCL in both the total score ($r = 0.49$; $P < .01$) and internalizing score ($r = 0.36$; $P < .05$), whereas a poor correlation was found between SDSC total score and externalizing score ($r = 0.28$; $P > .05$) approximately 50% of children with an abnormal total score on CBCL had an abnormal SDSC total score.

4. Discussion

Several studies have reported a higher incidence of sleep disorders in children with CP compared to typically developing children [6,11,12,22,23]. In our study, we found that more than 40% of children with CP presented with at least one sleep disorder, with a much higher incidence than in the normal population (5%) [5], when using the a tool previously used in different chronic diseases

Table 3
Child Behavior Checklist findings in the different groups of cerebral palsy patients.

	Diplegia	Hemiplegia	Quadriplegia	Dyskinesia	*P* value
CBCL internalizing	57 (49–64)*	58.5 (47.5–65)	49 (42–59)	64 (45–75)	.021
CBCL externalizing	49 (45–53)	53 (46–58)	44 (40–52)	52 (43–55)	.003
CBCL total	55.5 (49–61)	55.5 (46.5–64.5)	53 (45.5–59.5)	60 (43–70)	.297

Abbreviation: CBCL, Child Behavior Checklist.
* Data are expressed in median (interquartile range).

Table 4
Univariate analysis of associations between the independent variables and abnormal total scores on the Sleep Disturbance Scale for Children.

	Crude OR (95% CI)	Adjusted for diagnosis OR (95% CI)
Gender		
Boys	0.716 (0.300–1.732)	0.79 (0.35–1.78)
Age (y)		
6–7 (baseline)	–	–
8–12	0.984 (0.389–2.389)	0.88 (0.33–2.33)
13–19	0.857 (0.319–2.150)	0.83 (0.3–2.3)
IQ		
In reference range (baseline)	–	–
Borderline	0.464 (0.050–2.137)	1.43 (0.23–8.76)
Mental retardation	**4.060 (1.482–12.826)***	**4.13 (1.13–15.18)**
Epilepsy		
Controlled	**3.000 (1.236–7.425)**	**2.6 (1.06–6.38)**
Active	**3.500 (1.385–8.688)**	**3.22 (1.18–8.78)**
CBCL		
Internalizing	**5.636 (1.856–16.655)**	**7.44 (2.52–22)**
Externalizing	**26.800 (2.748–1276.275)**	**37.02 (3.69–370.68)**
Total	**11.909 (2.833–57.394)**	**18.03 (4.36–74.56)**
GMFCS		
1 (baseline)	–	–
2	0.464 (0–050–2.137)	0.57 (0.09–3.8)
3	0.224 (0.005–1.549)	0.36 (0.03–4.35)
4	0.960 (0.166–3.795)	1.38 (0.07–25.52)
5	**3.500 (1.385–8.688)**	3.67 (0.24–56.86)

Abbreviations: OR, odds ratio; CI, confidence interval; y, years; IQ, intelligence quotient; CBCL, Child Behavior Checklist; GMFCS, Gross Motor Function Classification System.
* Significant results ($P < .05$) are indicated in bold.

Table 5
Multivariable analysis of variables associated with an abnormal total scores on the Sleep Disturbance Scale for Children.

	OR (95% CI)
IQ: mental retardation	3.062 (0.829–11.31)
Epilepsy: active	2.041 (0.647–6.434)
CBCL internalizing	**5.793 (1.637–20.50)***
CBCL externalizing	**21.79 (2.021–235.0)**
GMFCS level 5	2.668 (0.789–9.023)

Abbreviations: OR, odds ratio; CI, confidence interval; IQ, intelligence quotient; CBCL, Child Behavior Checklist; GMFCS, Gross Motor Function Classification System.
* Significant results ($P \leqslant .05$) are indicated in bold.

(SDSC) [24–28]. There was no significant difference in SDSC total score among the four types of CP, but we observed that children with dyskinetic CP had higher scores on the SWTD and SHY factors: the SWTD factor included items related to hypnic jerks, rhythmic movement disorders, hypnagogic hallucinations, nocturnal hyperkinesias, and bruxism; and SHY factors included falling asleep sweating and night sweating. Motor problems of the dyskinetic form of CP could lead to a motor restlessness during sleep linked to a dopaminergic dysfunction or to a lesion of the basal ganglia, which could account for the hyperkinesia, hypnic jerks, rhythmic movement disorders, and bruxism [29,30].

Newman et al. [6] previously used the SDSC in 173 children with CP. Although there were differences in the population with younger age, lower incidence of epilepsy, and lower number of children with quadriplegia in that study, we found a similar prevalence of sleep disorders with a strong association between the SDSC total scores and epilepsy. The precise nature of the relationship between sleep disorders and epilepsy is complex. Epilepsy has frequently been reported as the main factor influencing sleep structure and sleep disturbances. Seizures could interfere with nighttime sleep structure and cause excessive daytime somnolence and sleep deprivation influences seizures [6,30,31]; furthermore, antiepileptic drugs can affect sleep quality and daytime alertness [30]. We found an abnormal SDSC total score in 34% of children with CP and active epilepsy vs 18% in children with CP and controlled epilepsy and 15% in children with CP without epilepsy. All the children with epilepsy (controlled or active) received antiepileptic treatment, and we did not observe any specific association with the type of antiepileptic agent, confirming previous findings that sleep disorders are more strongly associated with persistent seizures than with antiepileptic drugs [6]. We identified further clinical factors associated with an abnormal SDSC total score such as mental retardation and level 5 on the GMFCS.

Sleep disturbances are common in children with intellectual disabilities, but it is still debated if sleep disturbances are related to the associated neurologic impairments or directly linked to mental retardation, even if an alteration of nonrapid eye movement sleep and rapid eye movement sleep and of spindles in sleep of mentally retarded subjects has been reported with possible

Table 6
Sleep Disturbance Scale for Children scores and associated clinical factors.

	SDSC total	DIMS	SBD	DA	SWTD	DOES	SHY
	⩾70	⩾70	⩾70	⩾70	⩾70	⩾70	⩾70
GMFCS							
Level 5 (n = 41)	15	16	8	1	11	9	6
IQ							
In reference range (n = 54)	5	6	16	6	3	4	2
Borderline (n = 20)	2	5	4	3	1	3	0
Mental retardation (n = 91)	24	25	3	7	21	14	9
Epilepsy							
Absent (n = 102)	13	18	12	13	11	8	7
Controlled (n = 22)	4	3	4	1	5	3	0
Active (n = 41)	14	15	7	2	9	10	4
CBCL total score							
Abnormal (n = 39)	20	19	10	9	11	11	4
Normal (n = 126)	11	20	14	7	10	7	7

Abbreviations: SDSC, Sleep Disturbance Scale for Children; DIMS, difficulty in initiating or maintaining sleep; SBD, sleep-breathing disorders; DA, disorders of arousal; SWTD, sleep–wake transition disorders; DOES, disorders of excessive somnolence; SHY, sleep hyperhidrosis; CBCL, child behavior checklist; GMFCS, gross motor function classification system; IQ, intelligence quotient.

Table 7
Antieplipetic treatment in children with abnormal total scores on the Sleep Disturbance Scale for Children.

	VPA	CBZ	BDZ	PB	VGB	LEV	TPM	LTG
Active epilepsy	8	0	7	5	3	3	2	1
Controlled epilepsy	3	1	0	0	0	0	0	0

Abbreviations: VPA, valproate; CBZ, carbamazepine; BDZ, benzodiazepine; PB, phenobarbital; VGB, vigabatrin; LEV, levetiracetam; TPM, topiramate; LTG, lamotrigine.

linking to the level of mental retardation [7,8]. The results of our study confirm these data as 77% of children with an abnormal SDSC total score showed a mental retardation, whereas no clear relation has been reported in children with borderline or a normal level of IQ. Not surprisingly, the 48% of children with an abnormal SDSC total score showed a level 5 on the GMFCS. These patients showed a severe functional motor impairment often characterized by quadriplegia, experiencing pain related to stiffness and contractures, and behavioral, psychologic, and adaptive difficulties.

In our study we also were interested in establishing the possible relationship between behavior and sleep disorders, as behavioral and psychiatric problems are common in children with CP [15,32–34] and the association between behavior and sleep disorders has been largely reported in nondisabled children [35]. We choose the CBCL to assess behavior problems, a questionnaire performed by parents, which often is used even in severe CP [15,33]. In our cohort, 24% of the children reported an abnormal CBCL total score, with 27% showing internalizing and 9% showing externalizing problems. In agreement with previous studies [15,32–34], externalizing disorders as aggression and attention problems were more common in children with hemiplegia and dyskinetic CP than in those with quadriplegia and diplegia. Children with dyskinetic CP more frequently had internalizing disorders such as withdraw and somatic concerns than children with other types of CP. Behavioral problems often were associated with abnormal SDSC total score, as confirmed both by multivariate analysis and the correlation between SDSC total score and total and internalizing CBCL scores.

One of the weaknesses of our study was the lack of an age-matched control group of typically developing children, which would have allowed more detailed analysis on possible differences with CP children. However, the availability of Italian age-matched normative data with clear cutoff points allowed us to obtain reliable information on the number of the CP children outside the range reported as normal in the reference data.

Our results confirm that sleep disorders are common in children with CP and that different factors, such as motor or cognitive impairment, behavioral problems, or epilepsy, are important risk factors for the development of sleep disorders. Although none of these factors alone were associated with sleep disorders, the risk for developing abnormal patterns of sleep significantly increased with their presence. This relationship should be further explored in a larger sample to better understand how these factors influence each other and to establish possible causal relationships in more details.

Furthermore, because we used screening questionnaires (SDSC, CBCL), a more structured in-depth interview or objective assessment may have provided more adequate information on both psychiatric and sleep disorders [36] and allowed a more accurate diagnosis. A better understanding of these mechanisms will increase the opportunity to identify effective treatments to improve the well-being of the child and also the well-being of the family [37,23]. No sleep interventions specifically designed to improve the sleep of children with CP are reported in the literature, and only melatonin remains a commonly prescribed drug for disturbed sleep in children with neurologic dysfunction [38]. Further clues also may develop from the correlation with brain imaging and the pattern of brain lesions underlying CP, as few studies have reported that specific brain damage or hypoxic events, which are a common cause of CP, could affect sleep architecture [11,39,40].

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2013.08.793.

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